REMARKS

The present Preliminary Amendment is being filed to correct typographical errors in the specification.

Additionally, a copy of the English translation of the International Preliminary Examination Report is being submitted concurrently.

Examination of the application on its merits is respectfully requested.

Respectfully submitted,

Date: April 30, 2002

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ATTACHMENT -- CHANGES MADE TO THE SPECIFICATION

This attachment shows how certain paragraphs in the specification that were rewritten in this Preliminary Amendment differ from the previous version of these paragraphs, with underlining being used to identify added language, and brackets being used to identify deleted language.

The paragraphs beginning at page 11, line 18, and ending at page 12, line 8, have been changed as follows:

20 μ g type IV collagen was lysed in 1 ml phosphate buffered solution (PBS), and this lysate solution was used at 50 μ 1/well, and after coating a 96-well microplate (Falcon; Becton Dickinson Labware) at [4 C°] 4° C for overnight, was washed three times with PBS containing 0.05% Tween 20 and 0.1% BSA, and then blocked with PBS containing 0.2% BSA at 250 μ 1/well at [4 C°] 4° C overnight.

The serum obtained from the blood mentioned above was then diluted to 400 to 20000 times, and the diluted serum was added to the aforementioned 96-well microplate at 50 μ 1/well, and allowed to react at [4 C°] 4° C overnight. After the reaction, the 96-well microplate was washed three times with PBS containing 0.05% Tween 20, added 50 μ 1 of horseradish peroxidase (Sigma Chemical Co.)-conjugated goat anti-mouse IgG1, IgG2a, or IgG2b diluted to 200 times, and was then incubated at [4 C°] 4° C for 2 hours. After incubation, it was washed again three times with PBS containing 0.05% Tween 20, and developed enzyme reaction at room temperature for 30 minutes with 0.1 ml of True Blue Peroxidase Substrate (Kirkegaard & Perry Labs). The OD 450 was then read by using a Microplate Reader (Biolumin960; Molecular Dynamics Japan, Inc.). The results are shown in Fig. 3.

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Translation

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference A031-24PCT	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/JP00/04132	International filing date (*day/month/year*) 23 June 2000 (23.06.00)	Priority date (*day/month/year*) 25 June 1999 (25.06.99)
International Patent Classification (IPC) or national classification and IPC A01K 67/027, A61K 45/00, A61P 11/00, 13/12, G01N 33/50, 33/15, C12Q 1/68, C12N 15/12		
Applicant JAPAN SCIENCE AND TECHNOLOGY CORPORATION		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 4 sheets, including this cover sheet.

☐ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of _____ sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☒ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
17 January 2001 (17.01.01)	06 June 2001 (06.06.2001)
Name and mailing address of the IPEA/JP Facsimile No.	Authorized officer Telephone No.

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/JP00/04132

I. Basis of the report

1. With regard to the **elements** of the international application:*

☒ the international application as originally filed

☐ the description:

pages _____, as originally filed
pages _____, filed with the demand
pages _____, filed with the letter of _____

☐ the claims:

pages _____, as originally filed
pages _____, as amended (together with any statement under Article 19
pages _____, filed with the demand
pages _____, filed with the letter of _____

☐ the drawings:

pages _____, as originally filed
pages _____, filed with the demand
pages _____, filed with the letter of _____

☐ the sequence listing part of the description:

pages _____, as originally filed
pages _____, filed with the demand
pages _____, filed with the letter of _____

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.
These elements were available or furnished to this Authority in the following language _____ which is:

☐ the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).

☐ the language of publication of the international application (under Rule 48.3(b)).

☐ the language of the translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

☐ contained in the international application in written form.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority in written form.

☐ furnished subsequently to this Authority in computer readable form.

☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. ☐ The amendments have resulted in the cancellation of:

☐ the description, pages _____

☐ the claims, Nos. _____

☐ the drawings, sheets/fig _____

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).**

* *Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rule 70.16 and 70.17).*

** *Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.*

IV. Lack of unity of invention

1. In response to the invitation to restrict or pay additional fees the applicant has:

☐ restricted the claims.

☐ paid additional fees.

☐ paid additional fees under protest.

☐ neither restricted nor paid additional fees.

2. ☐ This Authority found that the requirement of unity of invention is not complied with and chose, according to Rule 68.1, not to invite the applicant to restrict or pay additional fees.

3. This Authority considers that the requirement of unity of invention in accordance with Rules 13.1, 13.2 and 13.3 is

☐ complied with.

☒ not complied with for the following reasons:

The special technical feature of claims 1-7 relates to a non-human Goodpasture's syndrome model animal, and the special technical feature of claim 8 relates to the early finding of Goodpasture's syndrome using human test cells. Since there is no technical relation between these inventions involving one or more of the same or corresponding technical features, these inventions are not so linked as to form a single general inventive concept.

4. Consequently, the following parts of the international application were the subject of international preliminary examination in establishing this report:

☐ all parts.

☐ the parts relating to claims Nos. _____.

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	1-8	YES
	Claims		NO
Inventive step (IS)	Claims		YES
	Claims	1-8	NO
Industrial applicability (IA)	Claims	1-8	YES
	Claims		NO

2. Citations and explanations

Document 1: Nature (T. Takai et al.), 1996, Vol. 379, pages 346-349
Document 2: J. Exp. Med. (T. Yuasa et al.), January 1999, Vol. 189 (1), pages 187-194
Document 3: Proc. Natl. Acad. Sci. USA, (R. Kalluri et al.), 1994, Vol. 91, pages 6201-6205

(1) Claims 1 and 2

Document 1 discloses that (1) since a mouse devoid of immunoglobulin Fcγ receptor IIB gene function shows a rise in the immunoglobulin level against an antigen, immunoglobulin Fcγ receptor IIB is a factor for negatively controlling the immune complex induction activity, and (2) its clarification is effective for developing therapeutic methods for autoimmune diseases. Document 2 discloses that if a mouse devoid of immunoglobulin Fcγ receptor IIB gene function is immunized with type II collagen, a crisis of type II collagen induced arthritis (CIA) as an autoimmune disease occurs. Document 3 discloses that the autoimmune reaction to type IV collagen induces Goodpasture's syndrome.

A person skilled in the art could have easily conceived from the disclosures of documents 1 and 2 that also in the case where a mouse devoid of immunoglobulin Fcγ receptor IIB gene function is immunized with type IV collagen that is an autoimmune disease inducing antigen like type II collagen (document 3), a crisis of an autoimmune disease (Goodpasture's syndrome) would occur in the mouse.

So, the subject matters of claims 1 and 2 do not appear to involve an inventive step in view of documents 1-3.

(2) Claims 3-7

Administering pathogenic model animals with test substances as screening to search for a therapeutic agent is a conventional means.

So, the subject matters of claims 3-7 do not appear to involve an inventive step in view of documents 1-3.

(3) Claim 8

Since the disclosures of documents 1 and 2 suggest that the lack of immunoglobulin Fcγ receptor IIB gene function is a cause of autoimmune diseases, it is considered to be obvious for a person skilled in the art to examine the lack of immunoglobulin Fcγ receptor IIB gene function for diagnosis of Goodpasture's syndrome.

So, the subject matter of claim 8 does not appear to involve an inventive step in view of documents 1 and 2.